UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

FEDERAL TRADE COMMISSION, Plaintiff, v. DIRECT MARKETING CONCEPTS, INC., et al, Defendants	CIVIL ACTION NO. 04-CV 11136GAO

DECLARATION OF STEFAN KRAAN, hDip, BSc. MSc, PhD.

I. Stefan Kraan, hereby declare as follows:

Introduction

1. I am a Post Doctoral Researcher at the Martin Ryan Institute, National University of Ireland, Galway. I am a Phycologist with 16 years of experience of marine algae, both in pure research and applied research.

2. During these 16 years I have studied a diverse range of subjects in phycology ranging from molecular biology of seaweeds to nutritive value of seaweeds.

3. I established and became Manager of the Irish Seaweed Centre (ISC; www.irishseaweed.com) in 2001, a centre for applied seaweed-based research and development, which was launched in 2001 as an initiative of the Department of the Marine (Irish Government), the Marine Institute, Irish Fisheries Board, Údarás na Gaeltachta and the National University of Ireland, Galway.

4. The Mission Statement of the Irish Seaweed Centre: '*The Irish Seaweed Centre is committed to initiating seaweed research projects, disseminating information regarding seaweed uses and applications and developing the sustainable seaweed resources in*

maritime areas. In addition, it will strengthen existing linkages and develop new alliances with other research centres and industry.'

5. In addition to my duties as Manager I act as the National Seaweed Research Coordinator for Ireland, I am co-founder of two companies both using seaweeds in product development one in the transport sector and one for nutritional value in the aquaculture sector.

Qualifications

6. I graduated with a MSc. degree in Marine Botany at University of Groningen, The Netherlands.

7. I obtained a PhD in phylogenetics and aquaculture of edible brown seaweed *Alaria esculenta* at the National University of Ireland, Galway (1998-2001). A true and accurate copy of my curriculum vitae is attached as Exhibit A.

8. I became manager of the Irish Seaweed Industry Organisation (ISIO) in 1998. The ISIO, consisting of members of the industry and external agencies, represents the Seaweed Industry at a local, national and international level.

9. I have conducted and coordinated many studies (national and International) on applied phycology, and written original articles published in peer-reviewed journals and books concerning seaweeds.

10. I am a member of the International Society of Applied Phycology (ISAP) and of the International Seaweed Association. Most recently I gave a presentation on nutritional value of seaweeds in aquaculture feeds in China, during the ISAP annual convention in August 2005 and will be presenting a keynote speech at the IFOAM Organic world

Congress 2005, Shaping Sustainable Systems on 22nd of September 2005, Adelaide, Australia.

11. Furthermore I am a member of the Kelp harvesting working group, the Marine Foresight forum and the National Seaweed Forum.

12. In the last four years I have been partner and coordinator of 10 national and 4 EU projects and over this period attracted over 2 million in research funding.

13. I have served as a reviewer for:

- Phycologia, an internationally renowned journal of marine botanical sciences
- MarLIN www pages; database on marine life, Marine Biological Ass. UK, Plymouth Phycological Research, Journal of the Japanese Society of Phycology
- Aquaculture International, an internationally renowned journal of aquacultural sciences
- Journal of Phycology: an internationally renowned journal of botanical sciences
- Journal of Applied Phycology: an internationally renowned journal dedicated to applied phycology

14. I have in my possession and have read the transcript of the Sea Vegg television advertisement version which was submitted in U.S. court documents by the Federal Trade Commission.

Relationship with FarmaSea® Health LLC. FarmaSea Pristine Ocean Blend™

15. I have known Scott Kennedy, President of FarmaSea for 5 years and have worked closely with Mr. Kennedy as a scientific advisor regarding the seaweeds used in the FarmaSea Pristine Ocean Blend in view of the nutritional value, time of harvesting, and

blend of species. Mr. Kennedy and FarmaSea Health LLC have been committed to providing a safe and all natural seaweed supplement to the masses.

16. I have acted as a liaison between FarmaSea Health LLC and the many seaweed harvesters and processors in the west of Ireland. The seaweeds used in the FarmaSea Pristine Ocean Blend have been selected from Ireland for a specific reason.

17. Ireland has very little industry, and the Irish west coast is still a pristine marine environment with **no** pollution. This is also clear from the Certificate of Analysis for FarmaSea Pristine Ocean Blend, showing that it contains no toxic heavy metals or microbial contaminants.

18. Ireland due to its location and climate is a hot spot for seaweed biodiversity in the world and has over 620 species recorded (Hardy & Guiry 2003). FarmaSea Pristine Ocean Blend contains a variable combination of 12 seaweed species harvested according to seasonal availability along the Irish coast selected from a total of 15 edible species. These species have been selected due to their nutritive value and the FarmaSea Pristine Ocean Blend contains a combination of at least 20% green seaweed, 30% red seaweeds and 50% brown seaweeds.

Safety and Formulation

19. For proprietary reasons the exact species formulation and levels will not be revealed in my affidavit. The species chosen in the FarmaSea Pristine Ocean Blend are Generally Recognized as Safe (GRAS) and have been approved for human consumption as non–traditional food substances under current EU legislation. The seaweeds used in FarmaSea Pristine Ocean Blend are harvested from the Irish west coast, rinsed with fresh

water, dried according specific protocols and milled to specifications supplied by FarmaSea Health LLC and Scott Kennedy.

20. Other than a natural flowing agent and whole plant filler (to stay within the iodine limits set by the FDA, which oddly enough is not based on any sound scientific evidence, as organic iodine is indeed a very important element for proper thyroid function), the proprietary milled blend of seaweeds from the Irish west coast are encapsulated and are not treated, heated or processed.

21. Nothing of the milled seaweed blend has been taken away or altered either (bio) chemically or mechanically. Therefore, the product Sea Vegg is whole sea vegetation (blends of edible milled seaweeds from the Irish west coast) in proprietary and safe amounts, and can be considered a definitive dietary food supplement.

22. Respectfully, the scientific findings and results related to studies on human dietary intake of the chosen species of sea vegetation can and should be applied to Sea Vegg, the product. I understand this is not true of most dietary supplements, which are fundamentally changed through chemical synthesis, standardizing extracts, deriving processes, concentration processing, freeze drying, chemically preserving, binding and others human and chemical interventions. Many of the "claims" for Sea Vegg/FarmaSea Pristine Ocean Blend/Irish seaweeds can be found herein. This document however, does not constitute the entire body of evidence regarding these powerful plants.

Traditional Background of seaweed consumption in Ireland

23. Seaweed harvesting and consumption has a long standing tradition in Ireland. The earliest record of collection of algae for food in Ireland appears to be in a stanza of a poem now thought to be 12th century describing monks harvesting the red alga *Palmaria*

palmata (Dillisk or Dulse) from the rocks and distributing this to the poor as one of their daily duties (Ó Madagáin 1994). Indeed *Palmaria palmata* has been used as food or medicine in Ireland over the last centuries, e.g., in the 18th century *Palmaria palmata* was used as chewing tobacco, vermifuge and commended against woman's longing (Threlkeld 1762).

24. Being rich in minerals, vitamins, trace elements and bioactive substances, seaweeds are called the medical food of the 21st century. Irish Moss or Carrageen (*Chondrus crispus*) has a large number of medical applications, some of which date from the 1830s. In Ireland it is still used to make traditional medicinal teas and cough medicines, to combat colds, bronchitis, and chronic coughs. It is said to be particularly useful for dislodging mucus and has anti-viral properties.

25. Carrageenan is also used as a suspension agent and stabiliser in other drugs, lotions and medicinal creams. Other medical applications are as an anticoagulant in blood products and for the treatment of bowel problems such as diarrhea, constipation and dysentery. It is also used to make internal poultices for the control of stomach ulcers (Morrissey *et al*. 2001).

26. In Ireland during the 17th century kelps were used as raw material for extraction of Iodine and have treated iodine deficiency goitre with iodine obtained from *Laminaria*. Brown algae in general are very high in iodine content up to 0.7 % of the wet weight. The uptake of dietary iodide (I-) by the human and animal thyroid glands leading to thyroid hormone formation is a well-established phenomenon. Up to 40-50 years ago these seaweed remedies were anecdotal information. Fortunately since the early sixties numerous scientific studies have now proven these health claims.

General overview of scientific backed health claims of Irish seaweed species used in FarmaSea Pristine Ocean Blend

27. Although not referenced in the advertisement, new research on the biocide properties of *Chondrus crispus* point to potential prophylactic action against HIV/AIDS. Applications of Carrageenan gels from *Chondrus crispus* can actually block the transmission of the HIV virus as well as other STD viruses such as gonorrhea, genital warts and the herpes simplex virus (Shanmugam & Mody 2000).

28. Massive clinical trials by the Population Council Centre began in 2002 in two severely-affected African countries, Botswana and South Africa. A carrageenan-based vaginal microbicide called Carraguard has been shown to block HIV and other sexually transmitted diseases in vitro. Carraguard entered phase III clinical trials involving 6000 non-pregnant, HIV-negative women in South Africa and Botswana in 2003 (Spieler, 2002).

29. An antitumorogenic role of kelp species or its equivalent iodine content in inhibiting tumorogenesis in rats with carcinogen induced mammary tumours has been reported (Funahashi *et al*. 1999).

30. It has also been shown that the high dietary seaweed content account for the relatively low prevalence of breast cancer in Japanese women (Cann *et al*. 2000). Like all kelp *L. digitata* is rich in iodine and is widely used as a health supplement for under-active thyroids (myxoedema), and for the treatment of goitre.

31. Besides high iodine levels kelp contain 40-50% of the dry weight in carbohydrates like fucoidans and laminarins and other polysaccharides all with their own

specific mode of action and benefits. Fucoidan and laminarin levels in Irish brown algae fluctuate between 4-7% of the dry weight (depending on season).

32. Fucoidan and laminarin of brown algae are isolated and charcterised by the Biochemistry Department, National University of Ireland, Galway together with a commercial partner for potential exploitation. Fucoidans, first isolated by Kylin (1913) almost one century ago, are sulphated polysaccharides (Fucans) extracted from kelp and have interesting bioactivities.

33. These polyanionic polysaccharides have antiangiogenesis, antiproliferation for tumor cells inhibition of tumour growth/reduction in tumour size (Ellouali *et al*, 1993) and more recently anti-inflammatory, anticoagulant, inhibition of the development of plasmodium in cell culture and inhibition of scavenger receptors that could lead to future applications in atherosclerosis treatments (Durig *et al*, 1997; Ying *et al*, 1997; Márcia *et al*, 2002).

34. Some anti-viral properties of sulphated fucans have also been characterized for example, inhibition of infection of human immunodeficiency virus but also inhibition of replication of other viruses like the Herpes Simplex Virus (Witvrouw and De Clercq, 1997).

35. The numerous important biological effects of fucoidans are related to their ability to modify cell surface properties (Usov *et al*, 2001). Their biological potential is linked to the number of sulphated molecules (role in the charge of the molecule) and the weight of the molecule. It is likely that some structural features are required for certain specific activities, such as, anticoagulant properties.

36. Laminarins provide protection against infection by bacterial pathogens, protection against severe irradiation and are able to boost the immune system by an increase of the B-cells and helper T-cells (Hoffman *et al.* 1996). Furthermore they provide protection against radiation damage, help in wound repair and reduce serum cholesterol levels and total serum lipid. Laminarin as a potential cancer therapeutic is under intensive investigation (Miao *et al.* 1999).

37. Aqueous extracts from two Irish red algae belonging to the Dumontiaceae have been found to inhibit the *herpes simplex* virus (Dieg *et al.* 1974; Ehresmann *et al.* 1979). However, no tests have been carried out on humans although a patent application has been filed in 2003 to use a pharmaceutical composition comprising floridoside from *Palmaria palmata* (present in the FarmaSea Pristine Ocean Blend) to inhibit viruses of the herpes family (US Pat. Appl. 20030181394).

38. *Digenea* sp are known to be high in kainic acid which works as an effective vermifuge. *Palmaria palmata* is used for the same reason (Michanek, 1979). Calciferous algae are used in Ireland to increase the daily intake of calcium. It is especially important in Osteoporosis, which is a debilitating disease charcterised by decreased bone mass and increased vulnerability to fractures which has been identified as a global public health problem affecting developed and developing Countries with consequences for both health and economics. Intake of Calcium and other minerals are essential for healthy bones however global dietary calcium intakes are not satisfactory and fall well below recommended levels. Several tablets and capsules are marketed in Ireland and abroad to increase calcium intake and specifically targets osteoporosis. These products are

marketed by Marigot Ltd and are patented under US 6,346,275 and EU Patent Application 98900971-7.

Mineral and vitamin properties of the FarmaSea Pristine Ocean Blend.

39. Seaweeds used in the FarmaSea Pristine Ocean Blend draw from the Atlantic Ocean an incomparable wealth of mineral elements, macro-elements and trace elements. The mineral fraction of some seaweeds in the blend accounts for up to 36% of dry matter. As concerns iodine, Kelp is the main source as it contains 1500 to 8000 ppm dry weight (Wracks contain 500 to 1000 ppm dry weight of iodine). Fucus vesiculosus is still registered in the European pharmacopoeia for its high iodine content.

40. Seaweeds are also one of the most important vegetable source of calcium. Calcium content may be as high as 7 % of the dry weight in species used in the Blend and up to 25 to 34 % in calcified seaweeds. Seaweed consumption may thus be useful in the case of expectant mothers, adolescents and elderly that all exposed to a risk of calcium deficiency

41. Specific mineral and vitamin contents of species used in Farmasea Pristine Ocean Blend are shown in Table 1-3. For proprietary reasons only a division into brown green and red seaweeds have been made. Levels are given for minimum and maximum values (season dependant) per division. Values have been obtained from the Irish Seaweed Industry, Teagasc (Irish State Agency), and the Irish Seaweed Centre.

Table 1. Brown Seaweeds:

Protein	5-20 %

Fat	2-4 %
Carbohydrates	42-64 %
Mannitol	4.2 %
Alginic acid	26 %
Laminaran	5-18 %
Fucoidan	4-7%
Vitamin A	0.7-0.8 ppm
Vitamin C	500-1650 ppm
B-Carotene	35-80 ppm
Vitamin B1	1-5 ppm
Vitamin B2	5-10 ppm
Vitamin B3	10-30 ppm
Vitamin B6	0.1-0.5 ppm
Vitamin B12	0.8-3 ppb
Vitamin E	260-450 ppm
Vitamin H	0.1-0.4 ppm
Vitamin K3	10 ppm
Calcium	1-3 %
Iodine	700-4500 ppm
Iron	101-176 ppm
Magnesium	0.5-0.9 %
Manganese	10-15 ppm

Sodium	3-4 %
Zinc	70-240 ppm

Table 2. Red seaweeds:

Protein	12-37 %
Fat	0.7-3 %
Carbohydrates	46-76 %
Carrageenan	40-45%
Vitamin C	130-1110 ppm
B-Carotene	266-384 ppm
Vitamin B1	3-7 ppm
Vitamin B2	2-29 ppm
Vitamin B3	2-98 ppm
Vitamin B6	9-112 ppm
Vitamin B12	6.6 ppb-20 ppm
Vitamin E	1.71 ppm
Calcium	2000-8000 ppm
Iodine	150-550 ppm
Iron	56-350 ppm
Magnesium	0.2-0.5 %

Manganese	10-155 ppm
Sodium	0.8-3 %
Zinc	3 ppm
Calcium	34%
Magnesium	2.4%
Phosphorus	0.8%
Sulphur	0.45%
Iron	25ppm
Manganese	125ppm
Boron	16ppm
Sodium	310ppm
Iodine	160ppm
Flourine	200ppm
Sodium	310ppm
Molybdenum	39ppm
Chromium	13ppm
Copper	10ppm
Zinc	37ppm
Aluminium	<5ppb
Nickel	30ppm
Cobalt	6ppm
Selenium	1ppm

Table 3. Green Seaweeds

Protein	10-25 %
Fat	0.5-1.7 %
Carbohydrates	42-48 %
Magnesium	2.8 %
Vitamin A	4286 I.U.
Vitamin C	40-200 ppm
Vitamin B3	98 ppm
Vitamin B12	6 ppm
Calcium	7300-9400 ppm
Iodine	70-240 ppm
Iron	152-1370 ppm
Manganese	12-347 ppm
Sodium	1.1-8.4 %

Specific mode of action of Minerals and vitamins (present in the FarmaSea Pristine Ocean Blend; after Arasaki & Arasaki, 1983; Nisizawa 2002).

41. In general, seaweeds (including the ones used in the FarmaSea Pristine Ocean Blend) contain 10 times as much of the below mentioned minerals compared to edible land plants. In certain cases (seaweed species dependant) even up to 50-100 times more. Below is a partial list of the vitamins, minerals, protein and phytonutrients contained in the Pristine Ocean blend:

- Calcium: Important for bones and teeth structure and muscle contractions. Cofactor for extracellular enzyme and proteins. Controls blood alkalinity and sustain normal working of the cardiac vessels. Seaweeds used in the Farmasea Pristine Ocean Blend econtain 10 times the amount of Calcium found in terrestrial plants.
- Phosphorous: Critical component in every body cell. Bone and membrane component. Essential energy carrier [ATP].
- Magnesium: Involved in more than 300 metabolic reactions [enzymatic regulation of lipid , carbohydrate and protein metabolism]. Important in cardiovascular function. Necessary for the conversion of blood sugar into energy and helps to relief stress.
- Iron: It is the key element in all living organisms. Regulates lipid and carbohydrate metabolism. Critical in oxygen transport in the blood.
- Sodium, Potassium and Chlorine: Electrolyte balance.
- Potassium is most abundant mineral found in the Farmasea Pristine Ocean Blend.
- It is vital for muscle contractions, nerve impulses and the proper functioning of heart and kidneys. Helps to regulate blood pressure and water balance in cells. High potassium diet may reduce the risk of hypertension and strokes.
- Manganese: needed for normal function and regeneration of central nervous system and is useful in preventing senile dementia.

- Zinc : Involved in catalytic, structural and regulatory functions. Stabilizes membranes, hormones and nucleic acids. Zinc accelerated wound healing. Deficiency may cause sterility and abnormal development of fetus.
- Copper: Cofactor in multiple enzymes. Connective tissue formation. Blood clothing. Energy conversion. Pigmentation of hair, skin and eyes.
- Iodine: Essential in thyroid's hormone function and therefore in weight control. Critical in the brain development in fetus and infants.
- Selenium: Present in Selenoproteins. Protects against oxidative injuries, such as, Arthritis. Organic selenium compounds are know to suppress the development of leukemia.
- Chromium: Regulates the function of insulin. Affects lipid metabolism.

Vitamin A:

42. Required for healthy eye function. Necessary for fetal development and strengthens the immune system.

Vitamin B1:

43. Necessary in nerve transmission. Its deficiency affects the cardiovascular, muscular, nervous and gastrointestinal systems.

Vitamin B2:

44. As a coenzyme, it participates in the redox reactions in the production of energy via the respiratory pathway.

Vitamin B3:

45. Function as nucleotide precursors which are key components in redox reactions.

Vitamin B6:

46. It has numerous complex functions: Sugar and fat metabolism, synthesis of neurotransmitters and hormone regulator.

Vitamin B12:

47. Functions as a coenzyme. Its deficiency causes anemia and neuropathy. Algae are a rich source of vitamins from group B For instance, seaweeds contain vitamin B12, which is particularly recommended in the treatment of the effects of ageing, of chronic fatigue syndrome (CFS) and anemia. Among the edible Irish seaweeds, the green algae are richest in vitamin B12 (used in FarmaSea Pristine Ocean Blend).

Vitamin C:

48. It functions as a protective antioxidant, necessary for the synthesis of connective tissue, important in neurotransmitter synthesis, involved in the regulation of iron metabolism. There are is scientific evidence that it strengthens the immune system, lower the risk of cancer and heart diseases. Seaweeds provide a worthwhile source of vitamin C (Qasim & Barkati 1985). The levels of Vitamin C average between 500 to 3000 mg/kg of dry matter for the green and brown algae (a level comparable with that of parsley, blackcurrant, and peppers), whereas the red algae contains vitamin C levels of around 100 to 800 mg/ kg. Vitamin C is of interest for many reasons: it strengthens the immune defense system, activates the intestinal absorption of iron, controls the formation of conjunctive tissue and the protidic matrix of bony tissue, and also acts in trapping free radicals and regenerates Vitamin E.

Vitamin E:

49. Functions as an anti-oxidant and prevents damage to membranes. protects PUFA. Due to its antioxidant activity, vitamin E inhibits the oxidation of the low-density

lipoproteins. It also plays an important part in the arachidonic acid chain by inhibiting the formation of prostaglandins and thromboxan. The brown seaweeds contain higher levels of vitamin E than green and red seaweeds. Among the brown algae, the highest levels are observed in the Fucaceae, Ascophyllum and Fucus sp., which contain between 200 and 600 mg of tocopherols / kg of dry matter. Brown algae contain alpha, beta and gamma tocopherols while the green and red algae only contain the alpha tocopherols. It was shown that the gamma and alpha tocopherols increase the production of nitric oxide and nitric oxide synthase activity (cNOS) and also play an important role in the prevention of cardio-vascular disease (Solibami et Kamat 1985).

Polysaccharides in the FarmaSea Pristine Ocean Blend (after Burtin et al. 2004)

50. Irish Seaweeds used in the FarmaSea Pristine Ocean Blend contain large amounts of polysaccharides, notably cell wall structural polysaccharides, such as, alginate from brown seaweeds and carrageenans from red seaweeds. Other minor polysaccharides are fucoidans (from brown seaweeds), xylans (from certain red and green seaweeds), ulvans in green seaweeds. Seaweeds also contain storage polysaccharides, such as, laminarin (B-1,3- glucan) in brown seaweeds and floridean starch (like glucan) in red seaweeds.

51. Among polysaccharides, fucoïdans are particularly studied as they showed interesting biological activities (anti-thrombotic, anti-coagulant, anti-cancer, anti-proliferative, anti-viral, and anti-complementary agent, anti-inflammatory, see below). These properties open up a wide field of therapeutic applications, some of which are already the subject of patents concerning notably the anti-coagulant and anti-thrombotic properties (Charreau et al. 1995, Nasu et al 1997, Angstwurm et al. 1997).

Proteins and amino acids in the FarmaSea Pristine Ocean Blend (after Burtin et al. 2004)

52. The protein content of brown seaweeds in the FarmaSea Pristine Ocean Blend is relatively small (average: 5-15 % of the dry weight), whereas higher protein contents are recorded in green and red seaweeds (on average 20-40 % of the dry weight). These levels are comparable to those found in high-protein vegetables such as soybeans (in which proteins represents 35 % of the dry mass). Several workers have described a high rate of algal protein degradation in vitro by proteolytic enzymes such as pepsin, pancreatin and pronase (Fujiwara-Arasaki 1979, Ryu et al. 1982). Among the algal proteins, it is worth noting the occurrence of phycobiliproteins in red algae (present in the FarmaSea Blend; Boussiba and Richmond 1979, Fan-jie et al. 1984). These compounds are made up of biline (tetrapyrolic open core) linked in a covalant way to a proteic chain. Recent studies showed that phycobiliproteins present antioxidant properties, which could be beneficial in the prevention or treatment of neuro-degenerative diseases caused by oxidative stress (Alzeimer's and Parkinson's) as well as in the cases of gastric ulcers and cancers (Gonzales et al. 1999, Padula et Boiteux 1999, Remirez et al. 1999).

53. The amino acids Tyrosine and histamine are of particular interest. The release of histamine is associated with an orgasm. Without adequate histamine releases, orgasm may be difficult or even impossible to achieve. Tyrosine is associated with lowering blood cholesterol.

Lipids and fatty acids in the FarmaSea Pristine Ocean Blend (after Burtin et al. 2004)

54. Lipids represent only 1-5 % of algal dry matter and show an interesting polyunsaturated fatty acid composition particularly in view of omega 3 and omega 6

acids which play a role in the prevention of cardio-vascular diseases, osteoarthritis and diabetes. The green algae show relatively high levels of alpha linolenic acid (Omega-3 C18:3). The red and brown algae are particularly rich in fatty acids with 20 carbon atoms: eicosapentanoic acid (EPA, Omega3 C20 :5) and arachidonic acid (AA , Omega6 C20 :4). Besides fatty acids, unsaponifiable fraction of seaweeds was found to contain carotenoids (such as B-carotene, lutein and violaxanthin in red and green seaweeds, fucoxanthin in brown seaweeds), tocopherols, sterols (such as fucosterol in brown seaweeds), and terpenoids (Jensen 1969, Piovetto et Peiffer 1991, Haugan et Liaaen-Jensen 1994). Lipidic extracts of these edible seaweeds showed antioxidant activity and a synergistic effect with the tocopherol (Le Tutour 1990).

Polyphenols or anti-oxidants

55. Irish sea vegetables used in the FarmaSea Pristine Ocean Blend are rich in polyphenols (anti-oxidants), highest contents are found in brown seaweeds, where phlorotanin range from 5 to 15 % of the dried weight (Ragan et Craigie 1973, Mc Innes et al 1984, Glombitza et Keusgen 1984). Antioxidant activity of polyphenols extracted from brown and red seaweeds has already been demonstrated by in vitro assays (Nakamura et al 1996). Studies have shown that there is a synergistic effect with Vit E (tocopherol; Le Tutour, 1990). Numerous laboratory studies have established that various polyphenols have significant antioxidant activity (Kalt et al., 2000).

56. After ingestion, various polyphenols have been detected in low concentrations in human blood plasma. Polyphenols have been traditionally thought of as having low bioavailability, but some studies have noted a significant increase in the antioxidant capacity of plasma following ingestion of these compounds in foods and beverages.

57. Epidemiological studies also note an association between a high intake of dietary polyphenols and lowered incidence of various chronic diseases (Arts et al., 2001). By helping to protect tissues against oxidative stress, certain polyphenols work as preventative medicines for problems such as cardiovascular diseases, cancers, arthritis, and autoimmune disorders. Some have also exhibited anti-inflammatory and hepatoprotective effects (Malikal et al. 2001; Garbisa et al., 2001).

Carotenoids

58. Carotenoids in the FarmaSea Pristine Ocean Blend are powerful antioxidants. Recent studies have shown the correlation between a diet rich in carotenoids and a diminishing risk of cardio-vascular disease, cancers (B-carotene, lycopene), as well as ophthalmologic diseases (lutein, zeaxanthin).

59. Irish brown seaweeds are particularly rich in carotenoids especially in fucoxanthin, B-carotene, violaxanthin. It has been demonstrated that fucoxanthin inhibits the proliferation of HL-60 cells (human Leukemia cell line) and induces their apoptosis (Hosokawa et al. 1999). The main carotenoids in the red algae are the B-carotene and A-carotene and their dihydroxylated derivatives: zeaxanthin and lutein. The carotenoid composition of the green algae is similar to that of higher plants: the main carotenoids present are the B-carotene, lutein, violaxanthin, antheraxanthin, zeaxanthin and neoxanthin. Numerous studies have demonstrated the antioxidant properties of the algal carotenoids and the role they play in preventing many pathologies linked to oxidative stress (Okuzumi et al 1993, Yan et al 1999).

Dietary fibres

60. Modern diets in the US are high in refined and processed foods and lack necessary dietary fibre. Seaweeds, like the brown algae used in the Pristine Ocean Blend contain 30-35% of the dry weight in soluble dietary fibres (alginates and fucoidans). These fibres help with clearing the digestive system in protecting surface membranes of the stomach and intestine from potential carcinogens. They absorb substances like cholesterol, which are then eliminated from the digestive system (Burtin et al, 2003).

61. Recent research in animals has shown that specific seaweed polysaccharides prevent proliferation of implanted cancer cells (Doi and Tsuji, 1998). These dietary polysaccharides are used in the FarmaSea Pristine Ocean Blend (alginates and fucoids in brown algae, sulfated galactans in red algae and rahmnan sulfates in green algae) and are not found in any land plants.

Antilipemic, hypocholesterolaemic, hypoglycemic, hypotensive and related activities of seaweed used in the Pristine Ocean Blend

62. There are various reasons why the blood pressure may be elevated however, high sodium intake and obesity aggravate this problem, both a major concern in the US. Large intake of salt (processed foods high in salt and fats) can lead to hypertension which can lead to arteriosclerosis and eventually to stroke or cardiac infarct. In Japan it is known that seaweeds in the diet lower blood pressure (Ren et al, 1994). Fucosterol (present in the Pristine Ocean Blend and only found in Seaweeds) is known to reduce lipids, amongst them LDL cholesterol, in the blood stream and lower blood pressure (Ren et al. 1994). A high level of LDL cholesterol can lead to plaque forming and clog arteries and

lead to cardiovascular diseases and heart attacks or strokes, a major cause of disease in the US.

63. Several macroalgal polysaccharides and fibres such as alginate, carrageenan, funoran, fucoidan, laminarin, porphyran and ulvan (all present in the FarmaSea Pristine Ocean Blend except funoran) have been noted to produce hypocholesterolemic and hypolipidemic responses due to reduced cholesterol absorption in the gut (Kiriyama et al., 1968; Lamela et al., 1989; Panlasigui et al., 2003). This is often coupled with an increase in the faecal cholesterol content and a hypoglycaemic response (Ito &Tsuchida, 1972; Nishide et al., 1993; Dumelod et al.,1999). Others have reported lowering of systolic blood pressure (antihypertensive responses) (Renn et al.,1994a, 1994b) and lower levels of total cholesterol, free cholesterol, triglyceride and phospholipids in the liver (Nishide & Uchida, 2003). Evidence suggests that ulvan as a dietary fibre plays a protective role in the rat such that it modulates the stimulatory effect of mucin secretion by goblet cells into the colon (Barcelo et al., 2000).

Cytotoxicity, antimitogenic, anticancer and antitumour properties of seaweed polysaccharides of the FarmaSea Pristine Ocean Blend

64. Several sulphated macroalgal polysaccharides have cytotoxic properties. Fucoidans (present in the FarmaSea Pristine Ocean Blend) are known to have antitumour, anticancer, antimetastatic and fibrinolytic properties in mice (Coombe et al., 1987; Maruyama et al., 1987) They also reduce cell proliferation (Religa et al., 2000). These

polyanionic polysaccharides have antiangiogenesis, antiproliferation for tumor cells inhibition of tumour growth/reduction in tumour size (Ellouali *et al*, 1993).

65. The numerous important biological effects of fucoidans are related to their ability to modify cell surface properties (Usov *et al*, 2001). Their biological potential is linked to the number of sulphated molecules (role in the charge of the molecule) and the weight of the molecule. Translam, the 1→3:1→6-β-D-glucans produced by enzymatic action on laminarin (present in FarmaSea Pristine Ocean Blend), has antitumour properties (Saito et al.,1992).

66. Laminarins provide protection against infection by bacterial pathogens, protection against severe irradiation and are able to boost the immune system by an increase of the B-cells and helper T-cells (Hoffman *et al*. 1996). Furthermore they provide protection against radiation damage, help in wound repair and reduce serum cholesterol levels and total serum lipid. Laminarin as a potential cancer therapeutic is under intensive investigation (Miao *et al*. 1999).

67. Moreover, it has been demonstrated that fucoxanthin (accessory pigment in photosynthesis in brown algae (used in the FarmaSea Blend) inhibits the proliferation of HL-60 cells (human Leukemia cell line) and induces their apoptosis (Hosokawa et al. 1999). Kaeffer et al. (1999) noted that ulvan (present in the FarmaSea Pristine Ocean Blend) has cytotoxicity or cytostaticity targeted to normal or cancerous colonic epithelial cells. Several studies using cell cultures and animal models of cancer prevention and treatment with seaweed and seaweed extracts support that seaweed is associated with decreased cancer incidence (Funahashi et al. 2001; Maruyama et al., 2003; Takahashi et al., 2000).

Anti-inflammatory activity and effects on the Auto-Immune response.

68. Macroalgae, especially red algae (see lipid and fatty acids paragraph above), are rich in 20-carbon atom polyunsaturated fatty acids (PUFAs), chiefly eicosapentaenoic and docosahexanoic acids (Stefanov et al., 1988; Gerwick & Bernart, 1993). Seaweeds are capable of metabolising various C20-PUFAs via oxidative pathways (Gerwick et al., 1993). In many red algae, the metabolised products of PUFAs, called oxylipins, resemble eicosanoid hormones in higher plants and humans which fulfill a range of physiologically important functions (Gerwick et al., 1993; Imbs et al., 2001). The anomalous production of these compounds underlies a number of diseases related to inflammation (Gerwick & Bernart, 1993), and so eicosanoids and their derivatives have received much research attention in the search for development of new classes of anti-inflammatory drugs (Jacobs et al.,1993).

69. Sulphated polysaccharides (fucans) extracted from kelp (present in FarmaSea Pristine Ocean Blend) have shown a anti-inflammatory, anticoagulant, inhibition of the development of plasmodium in cell culture and inhibition of scavenger receptors that could lead to future applications in atherosclerosis treatments (Durig *et al*, 1997; Ying *et al*, 1997; Márcia *et al*, 2002). Translam, 1→3:1→6-β-D-glucans produced from laminarin (present in FarmaSea Pristine Ocean Blend), has immunostimulating activities in animals and plants and it has been suggested that they might serve as radioprotective substances in patients with radiation illness (Kuznetsova et al., 1994; Zaporozhets et al., 1995; Chertkov et al., 1999). Preparations containing 1→3:1→6-β-D-glucans, laminarin, and fucoidan (all present in FarmaSea Pristine Ocean Blend) are manufactured by the health industry and marketed for their beneficial properties on the immune system. The

producers of these tablets cite numerous papers discussing the biological activities of the 1→3:1→6-β-D-glucans. Porphyran (present in FarmaSea Pristine Ocean Blend) likely contributes to macrophage stimulating activity in mice (Yoshizawa et al., 1995).

Non insulin dependent diabetes mellitus and glycemia

70. Glucose tolerance and insulin sensitivity are key-issues involved in the development of non-insulin dependent diabetes mellitus (NIDDM) in humans, a rising problem in many western developed countries. Soluble dietary fibers have been shown to improve glucose tolerance and insulin sensitivity. Vaugelade et al. (2000) reported while using alginates from Kelp (present in FarmaSea Pristine Ocean Blend) a dramatic reduction of glucose absorption balance and insulin response in the pig after a high carbohydrate test meal supplemented with 5% kelp fibers. They reported a 50% decrease of glucose absorption balance over 8 h. The latter results are consistent with previously reported observations on alginates. Alginates, at a low dose, induce a lower postprandial rise in peripheral blood glucose and serum insulin in NIDDM human subjects. Alginates inhibit blood glucose levels from rising 30 min after glucose administration in an oral glucose tolerance test performed in rats.

71. The post prandial glycemic response is also lowered in streptozotocin-induced diabetic rats receiving a diet containing 2.5% alginates (Vaugelade et al., 2000). Total available carbohydrate (sugars and starches) and total dietary fiber (soluble and insoluble) make up the total carbohydrate content of a food. Soluble fiber decreases the availability of glucose by delaying its absorption in the proximal small intestine, thus reducing the postprandial glucose levels (Jenkins et al. , 1978).

72. Carrageenan, a seaweed extract (present in the FarmaSea Pristine Ocean Blend), is a good source of soluble fiber (Burtin, 2003). The effect of carrageenan incorporation into arroz caldo on carbohydrate availability was studied by monitoring the postprandial blood glucose levels of human subjects (Dumelod et al., 1999). Control and experimental arroz caldo samples were prepared and subjected to proximate analysis and feeding studies. The total dietary fiber (TDF) content of the experimental feed (2.03%) was about thrice that of the control (0.68%).

73. Using randomized crossover design, preweighed 55g available carbohydrate serving portions of control and experimental arroz caldo samples, with 3.45 and 14.84 g TDF, respectively, were fed to ten fasting human subjects, after which their postprandial blood glucose levels were determined at 15, 30, 45, 60 and 90 min intervals. Results of the short-term in vivo study showed that the mean postprandial glycaemic responses of subjects after consuming the experimental sample were significantly lower than the levels after consuming the control at 15, 45, and 90 min (P 0.05) and at 30min (P 0.001). Likewise, the mean glucose area under the curve was significantly lower (P 0.01) after consumption of experimental arroz caldo than control. The hypoglycaemic effect of carrageenan may prove useful in the prevention and management of metabolic conditions such as diabetes (Dumelod et al., 1999).

Conclusions

74. The above described scientific evidence applies for chemical constituents of species used in the FarmaSea Pristine Ocean Blend and so the product Sea Vegg. Seaweeds (sea vegetables) used in the FarmaSea Pristine Ocean Blend are harvested from the Irish West Coast. Sea Vegg consists of whole non-treated and non-processed organic

sea vegetables, which are rinsed, dried, milled and encapsulated. Levels and exact species composition are not revealed due to proprietary reasons, although reference is made in the text of the proximate composition of brown, red and green algae. The seaweeds in the FarmaSea Pristine Ocean Blend exhibit original and interesting nutritional properties and can be used as an excellent source of truly natural minerals, vitamins, amino acids, polyphenols, anti-oxidants, plant sterols, lipids, carbohydrates, alginates, fibre, protein, fucoidans, laminarins, chlorophyll, kainic acid, and many other subsets of natural nutrition.

75. Strong and undeniable scientific evidence has been presented that these species possess **cytotoxicity, antimutogenic, anticancer and antitumour** properties and **anti-inflammatory, antilipemic, hypocholesterolaemic, hypoglycemic and hypotensive related activities**, when eaten whole or as a dietary food supplement on a daily basis.

76. Undeniable proof has been presented that these species possess other bioactive properties that help reduce symptoms, such as, **Non insulin dependent diabetes mellitus, glycemia, and oxidative stress related diseases.**

77. There is a strong scientific evidence and suggestion that daily intake of sea vegetation can actually help prevent cancer. This is dramatically shown in Asian studies in which daily intake is 7 grams of whole sea vegetables as part of the diet and is statistically correlated with a lower cancer incidence(Cann *et al*. 2000). The Japanese traditionally use as few as three and as many as five species in their diet.

78. In my professional opinion the FarmaSea Pristine Ocean Blend of sea plants, as contained unchanged in the product Sea Vegg, can and will have far reaching and

positive human biological value, when ingested as a daily regimen of nutrition, especially in those counties and communities struggling with malnutrition.

79. There are strong scientifically observed correlations between human biological homeostasis, and disease remission,treatment and prevention, especially in the case of degenerative (age related) disease.

I hereby declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Signed: _____ Date: 13 SEPTEMBER 2005.

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